CLAIMS

1. A Gram negative bacterium in which the expression of a protein involved in LPS transport to the outer membrane is functionally downregulated such that the level of LPS in the outer membrane is decreased compared to a wild-type Gram negative bacterium.

2. The Gram negative bacterium of claim 1, with the proviso that the Gram negative bacterium expresses Imp, in which the protein involved in LPS transport is Imp.

3. The Gram negative bacterium of claim 2 wherein the Imp expression is functionally downregulated by downregulating expression from an *imp* gene.

4. The Gram negative bacterium of claim 2 or 3 wherein the Imp expression is functionally downregulated by disrupting the structure of the Imp protein.

5. The Gram negative bacterium of claim 4 wherein at least one of the extracellular loops of the Imp protein is disrupted by inserting a sequence from a different protein into the loop to make a chimeric protein.

6. The Gram negative bacterium of claim 4 or 5 wherein the structure of the Imp protein is disrupted by removing part of the sequence of the Imp protein and optionally replacing it with a sequence from a different protein to make a chimeric protein.

7. The Gram negative bacterium of claim 6 wherein at least part of at least one extracellular loop of the Imp protein is removed and optionally replaced with a sequence from a different protein to make a chimeric protein

8. The Gram negative bacterium of any preceding claim, with the proviso that the Gram negative bacterium is not *E. coli,* in which the protein involved in LPS transport is MsbA.

9. The Gram negative bacterium of claim 8 wherein the MsbA expression is functionally downregulated by downregulating expression from an msbA gene.

10. The Gram negative bacterium of claim 8 or 9 wherein the MsbA expression is functionally downregulated by disrupting the structure of the MsbA protein

11. The Gram negative bacterium of any one of claims 1-10 wherein the bacterium is a Neisserial strain, preferably *Neisseria meningitidis*.

12. A chimeric protein comprising at least one part which is derived from an Imp protein and at least one part which is derived from at least one different protein.

13. The chimeric protein of claim 12 wherein at least one part derived from at least one different protein is inserted into at least one extracellular loop of Imp.

14. The chimeric protein of claim 13 wherein at least a portion of at least one extracellular loop from Imp is deleted and replaced with at least one part derived from at least one different protein.

15. The chimeric protein of claim 12 comprising at least one extracellular loop from an Imp protein linked to a polypeptide sequence from at least one different protein.

16. The chimeric protein of any one of claims 12-15 wherein the Imp protein is from a Neisserial strain, preferably *N. meningitidis*.

17. The chimeric protein of any one of claims 12-16 wherein the Imp protein part of the chimeric protein has a sequence sharing at least 80% identity with the corresponding sequence of SEQ ID No 1.

18. The chimeric protein of any one of claims 12-17 which has a sequence sharing at least 60% identity with the sequence of SEQ ID No. 1.

19. The chimeric protein of any one of claims 12-18 wherein the part derived from a different protein comprises an epitope capable of generating an immune response against a Neisserial protein.

20. The chimeric protein of any one of claims 12-19 wherein the chimeric protein has impaired LPS transporter function compared to the LPS transporter function of a wild-type Imp protein from which it is derived.

21. The chimeric protein of any one of claims 12-20 wherein the part derived from a different protein is inserted into loop 3 of Imp and optionally at least part of the loop 3 is deleted.

22. The chimeric protein of any one of claims 12-21 wherein an Imp sequence corresponding to amino acids 357-416 or a portion thereof of SEQ ID No. 1 is deleted and optionally replaced with a part derived from a different protein.

23. The chimeric protein of any one of claims 12-22 wherein the part derived from a different protein is inserted into loop 8 of Imp and optionally at least part of the loop is deleted.

24. The chimeric protein of any one of claims 12-23 wherein an Imp sequence corresponding to amino acids 648-697 or a portion thereof of SEQ ID No. 1 is deleted and optionally replaced with a part derived from a different protein.

25. The chimeric protein of any one of claims 12-24 wherein the part derived from a different protein is inserted into loop 6 of Imp and optionally at least part of the loop is deleted.

26. The chimeric protein of any one of claims 12-25 wherein an Imp sequence corresponding to amino acids 537-576 or portion thereof of SEQ ID No. 1 is deleted and optionally replaced with a part derived from a different protein.

27. The chimeric protein of any one of claims 12-26 wherein the part derived from a different protein is inserted into loop 2 of Imp and optionally at least part of the loop is deleted.

28. The chimeric protein of any one of claims 12-27 wherein an Imp sequence corresponding to amino acids 295-332 or portion thereof of SEQ ID No. 1 is deleted and optionally replaced with a part derived from a different protein.

29. The chimeric protein of any one of claims 12-28 wherein the part derived from a different protein is inserted into loop 1 of Imp and optionally at least part of the loop is deleted.

30. The chimeric protein of any one of claims 12-29 wherein an Imp sequence corresponding to amino acids 252-271 or portion thereof of SEQ ID No. 1 is deleted and optionally replaced with a part derived from a different protein.

31. The chimeric protein of any one of claims 12-30 wherein the part derived from a different protein is inserted into loop 5 of Imp and optionally at least part of the loop is deleted.

32. The chimeric protein of any one of claims 12-31 wherein an Imp sequence corresponding to amino acids 482-501 or portion thereof of SEQ ID No. 1 is deleted and optionally replaced with an insert part derived from a different protein.

33. The chimeric protein of any one of claims 12-32 wherein the part derived from a different protein is inserted into loop 9 of Imp and optionally at least part of the loop is deleted.

34. The chimeric protein of any one of claims 12-33 wherein an Imp sequence corresponding to amino acids 721-740 or portion thereof of SEQ ID No. 1 is deleted and optionally replaced with a part derived from a different protein.

35. The chimeric protein of any one of claims 12-34 wherein at least one part derived from a different protein, is a Neisserial, preferably a *N. meningitidis* protein.

36. The chimeric protein of claim 35 wherein at least one part is derived from PorA.

37. The chimeric protein of claim 36 wherein 2 or more parts are derived from 2 or more PorA proteins from different serosubtypes of N. meningitidis.

38. The chimeric protein of any one of claims 35-37 wherein at least one part is derived from Hsf.

39. The chimeric protein of any one of claims 35-38 wherein at least one part is derived from TbpA.

40. The chimeric protein of any one of claims 35-39 wherein at least one part is derived from TbpA –high molecular weight and at least one different part is derived from TbpA – low molecular weight.

41. The chimeric protein of any one of claims 35-40 wherein at least one insert part is derived from NspA .

42. The chimeric protein of any one of claims 35-41 wherein at least one part is a peptide mimotope of a Neisserial LOS.

43. The chimeric protein of any one of claims 35-42 wherein at least one part is derived from Hap.

44. The chimeric protein of any one of claims 12-43 wherein at least one part is derived from a S. pneumoniae protein.

45. The chimeric protein of any one of claims 12-44 wherein at least one part derived from a different protein is surface exposed in the bacterial strain from which it is derived.

46. A polynucleotide comprising a sequence encoding the chimeric protein of any one of claims 12-45.

47. An expression vector comprising the polynucleotide of claim 46.

48. A host cell comprising the expression vector of claim 47.

49. An outer membrane vesicle preparation in which the level of LPS is decreased compared to the LPS level in an outer membrane vesicle preparation derived from a wild-type parent strain and containing a functionally downregulated protein that is involved in the transport of LPS to the outer membrane in a parent Gram negative bacterium.

50. An outer membrane vesicle preparation derived from the Gram negative bacterium of any one of claims 1-11 or the host cell of claim 48 or comprising the chimeric protein of any one of claims 12-45.

51. The outer membrane vesicle preparation of claim 49 or claim 50 derived from *N. meningitidis* wherein the amount of LPS in the outer membrane vesicle is reduced compared to the amount of LPS in an outer membrane vesicle preparation derived from a strain of *N. meningitidis* where Imp or MsbA is not functionally disrupted.

52. The outer membrane vesicle preparation of any one of claims 49-51 wherein the level of LPS is sufficiently low so that the toxicity is reduced to a level at which the outer membrane vesicle preparation has an acceptable level of reactogenicity when inoculated into a patient.

53. The outer membrane vesicle preparation of any one of claims 49-52 wherein LPS present in the outer membrane vesicles is intra-vesicle cross-linked to outer membrane proteins in the outer membrane vesicle.

54. The outer membrane vesicle preparation of any one of claims 49-53 wherein the concentration of lipoproteins in the outer membrane vesicles is equivalent to the concentration of lipoproteins from outer membrane vesicles derived from a non-detergent extraction process.

55. A method for producing the chimeric protein of any one of claims 12-45 comprising the steps of culturing the host cell of claim 48 under conditions under which the chimeric protein is expressed and recovering the expressed chimeric protein.

56. A method for producing the outer membrane vesicle preparation of claim 49-54 comprising the step of culturing the host cell of claim 48 or the Gram negative bacterium of claims 1-11.

57. A pharmaceutical composition comprising the Gram negative bacterium of claims 1-11 or a fraction or membrane thereof, the chimeric protein of any one of claims 12-45 or

the outer membrane vesicle preparation of any one of claims 49-54, and a pharmaceutically acceptable carrier.

58. The pharmaceutical composition of claim 57 in the form of a vaccine.

59. The pharmaceutical composition of claim 57 or claim 58 further comprising one or more bacterial capsular polysaccharides or oligosaccharides.

60. The pharmaceutical composition of claim 59 wherein the one or more capsular polysaccharides or oligosaccharides is derived from bacteria selected from the group consisting of N. meningitidis serogroup A, C, Y and/or W-135, Haemophilus influenzae b, Streptococcus pneumoniae, and are preferably conjugated to a source of T-helper epitopes.

61. A method of preventing or treating Gram negative bacterial infection, preferably Neisserial infection by administering the chimeric protein of any one of claims 12-45 or the outer membrane vesicle preparation of any one of claims 49-54 or the pharmaceutical composition of any one of claims 57-60 to a patient in need thereof.

62. A use of the Gram negative bacterium of any one of claims 1-11 or a fraction or membrane thereof, the chimeric protein of any one of claims 12-45 or the outer membrane vesicle preparation of any one of claims 49-54 in the preparation of a medicament for treatment or prevention of Gram negative bacterial infection, preferably Neisserial infection.